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GB 2342292 A WO 99/45906 A1 US 5985891 A

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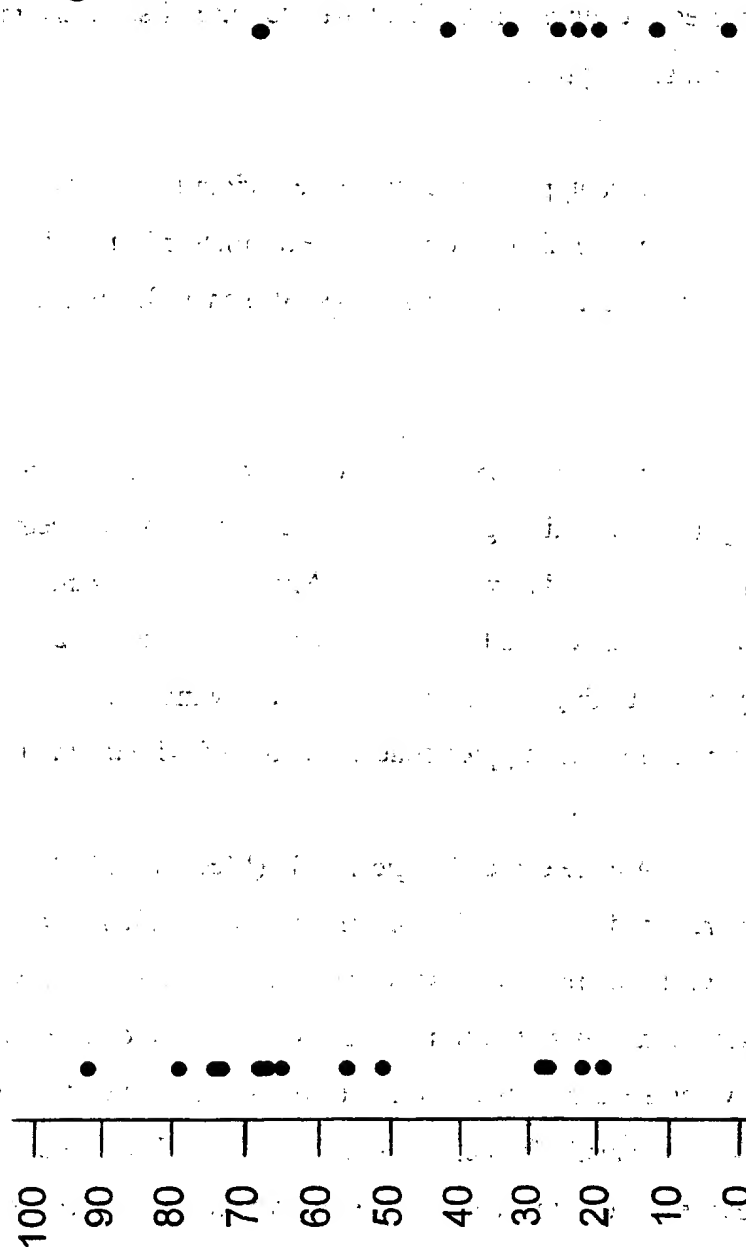
(54) Abstract Title

A medicament for the treatment of equine oral stereotypies using a pH regulator

(57) A pH regulator is used in a method of manufacture of a medicament for the treatment of equine oral stereotypies such as windsucking, cribbing and woodchewing. The pH regulator may be an antacid such as sodium carbonate, sodium hydrogencarbonate, magnesium hydroxide, calcium carbonate, calcium hydroxide and magnesium carbonate.

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Figure 1



ORAL STEREOTYPIES

The present invention concerns medicaments for the treatment of oral stereotypies in equines, methods of manufacture of same and methods of treatment of equine oral stereotypies.

Stereotypies are repetitive behaviour patterns which have no obvious goal or function, and are displayed by captive animals, mentally ill or handicapped humans and subjects administered certain drugs (Mason, G.J., 1991, *Anim. Behav.*, 41: 1015 - 1037).

In horses, stereotypies include windsucking (the repetitive gulping of air), cribbing (the repetitive grasping and pulling with the teeth of objects), weaving, boxwalking and woodchewing (see e.g. Mills, D.S. and Nankervis, K.J., 1999, "Equine Behaviour: Principles and Practise", Blackwell Science, pp. 210 - 225). Certain of these, namely windsucking, cribbing and woodchewing, can be regarded as being "oral stereotypies" i.e. stereotypies done or performed with the mouth.

A large epidemiological study (McGreevy, P.D. *et al.*, *Vet. Rec.*, 137: 36-37) has reported that over 7% of British National Hunt horses and more than 8% of British event and dressage horses engaged in either cribbing or windsucking. The figure in leisure horses is not absolutely known, but would appear to be about 5%. Such stereotypies are unsightly and oral stereotypies can cause teeth wear and may increase the risk of potentially fatal disorders such as colic. They are also an unsoundness which reduces the value of the horse on sale and which must be declared when the horse is put up for sale.

With an estimated population of 600,000 horses in the UK alone, there is naturally a significant desire to treat stereotypies, including oral stereotypies. Current treatments for oral stereotypies can be quite barbaric and include the use of electric currents on surfaces grabbed by a horse in order to shock them into stopping, surgery to remove the muscles involved in the behaviour and/or the nerves controlling them, and various types of strap which either hurt a horse or cut off its air supply when it tries to engage in the behaviour. These treatments are also found to be generally ineffective.

The present inventors have now developed an effective treatment for oral stereotypies in equines and compositions for same. This treatment has not previously been suggested, is therapeutically effective (as compared to the prior art) and does not involve causing any suffering to equines being treated.

According to the present invention there is provided the use of a pH regulator in a method of manufacture of a medicament for the treatment of equine oral stereotypies.

Experiments (below) demonstrate a highly significant reduction in exhibited oral stereotypies (for example crib-biting, also referred to as cribbing) post-feeding by horses who were fed the medicaments of the present invention.

The pH regulator may be an antacid. Antacids have previously been used in medicaments for equines and ruminants, but never in medicaments for treating oral stereotypies. US 5744178 discloses a ruminant feed additive containing phosphoric acid-amino acid-polyvalent metal composite salt and gastric antacids, the additive being stable in the rumen of a ruminant and which can release basic amino acids in the abomasum and lower digestive organs. The gastric antacids affect the pH in the rumen, increasing it to ensure that the composite salt remains insoluble. Upon entry of the composite salt into the abomasum the pH drops sufficiently to allow solubilisation of the composite salt. US

5391372 concerns methods for treating the symptoms of colic and founder in horses, and discloses that antacids have previously been used in the preparation of medicaments for treating colic.

The antacid may be a gastric antacid.

Also provided according to the present invention is a method of manufacture of a medicament for the treatment of equine oral stereotypies, characterised in the use of a pH regulator.

A wide range of antacid compounds are well known in the art, and include sodium carbonate, sodium hydrogencarbonate, magnesium hydroxide, magnesium oxide, potassium hydroxide, calcium carbonate, calcium hydroxide, and magnesium carbonate. Antacid preparations are extensively known, and typically comprise an antacid compound or compounds together with a pharmaceutically acceptable carrier, diluent or excipient (Remington's Pharmaceutical Sciences and US Pharmacopeia, 1984, Mack Publishing Company, Easton, PA, USA), and such preparations may be readily used in the present invention.

The pH regulator may comprise at least 50% of the therapeutically active ingredients (by weight) of medicaments according to the present invention. It may for example comprise at least 60, 70, 80, 90 or 95% of the therapeutically active ingredients of a medicament, and may even be the sole active ingredient.

By "therapeutically active ingredients" is meant ingredients of medicament of the present invention which cause a therapeutic effect. Thus pharmaceutically acceptable carrier, diluents and excipients are not considered to be therapeutically active ingredients.

The pH regulator may form at least 50% by weight of any medicaments according to the present invention, for example at least 60, 70, 80, 90 or 95%.

Also provided according to the present invention is a method of treatment of equine oral stereotypies, comprising administering to the equine a medicament according to the present invention.

The present invention is also considered to extend to the treatment of Oral Stereotypies in pigs and other simple stomached animals kept in captivity.

The medicaments of the present invention may be best administered immediately pre-feeding or at other times, depending upon the exact form the medicament takes - it is well known in the art to provide antacids in a "slow release" or "delayed release" formulation.

The exact doses of pH regulator to be administered may be readily determined using simple dose-response assays. The medicament may form part of the feed provided to the equine.

The efficacy of any medicament may also be affected by other conditions or factors. In particular, it has been found previously that stereotypies can persist even when their cause has been removed (Mason, G.J., 1991, *supra*). Therefore the medicaments of the present invention may be most effective when administered to an animal which has not established patterns of stereotypical behaviour. However, this does not preclude its efficacy in treating animals with established oral stereotypies - the experiments detailed below show the effective treatment of oral stereotypies in a horse which had displayed them for over 5 years.

The invention will be further apparent from the following description, with reference to the accompanying drawing, which shows, by way of example only, one form of treatment of oral stereotypies.

The Figure shows the number of crib-bites/windsucking occurrences during the ten minute period immediately post-feeding. X-axis shows (x=0) days without treatment and (x=1) days with treatment. Y-axis shows total number of crib bites/windsucking events.

A trial with was performed over the course of 24 days with a horse which displayed windsucking behaviour. On days 6,8,10 and 12-18 medicaments were administered to the horse. On other days no medicaments were administered. The medicaments comprised six Rennie (RTM) antacid tablets administered immediately pre-feeding. After feeding, the behaviour of the horse was observed for ten minutes. During the ten minute period, the number of crib bites and windsucks was counted, a general assessment of the level of cribbing/windsucking during the day as a whole made, and any other observations as to the horse's behaviour noted.

The results as analysed using a Kruskal-Wallis test showed that treatment did indeed cause a reduction in the occurrence or cribbing/wind sucking ($P=0.018$). The full results are given in Table 1. Column A is the day of the treatment; Column B whether treatment was with antacid (1) or no treatment (0); Column C is the total bites; and Column D is the general score.

Table 1

| A | B | C | Number Of Bites In Each Of Minutes | | | | | | | | | | D |
|----|---|----|------------------------------------|----|----|----|----|----|----|----|----|----|-----|
| | | | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | |
| 23 | 0 | 65 | 0 | 13 | 10 | 12 | 6 | 8 | 6 | 5 | 3 | 2 | 6.0 |
| 22 | 0 | 73 | 6 | 11 | 11 | 8 | 10 | 5 | 12 | 7 | 1 | 2 | 6.5 |
| 19 | 0 | 22 | 3 | 0 | 1 | 3 | 4 | 4 | 1 | 1 | 3 | 2 | 1.5 |
| 20 | 0 | 68 | 5 | 8 | 3 | 11 | 4 | 12 | 8 | 9 | 3 | 5 | 6.0 |
| 21 | 0 | 73 | 9 | 13 | 10 | 7 | 15 | 7 | 5 | 3 | 0 | 4 | 7.0 |
| 24 | 0 | 92 | 12 | 11 | 12 | 10 | 12 | 9 | 5 | 10 | 8 | 3 | 8.5 |
| 11 | 0 | 19 | 0 | 1 | 7 | 2 | 0 | 0 | 0 | 0 | 7 | 2 | 1.0 |
| 2 | 0 | 27 | 0 | 0 | 0 | 2 | 1 | 0 | 0 | 6 | 11 | 7 | 3.0 |
| 5 | 0 | 67 | 6 | 2 | 11 | 10 | 6 | 11 | 6 | 5 | 7 | 3 | 7.5 |
| 4 | 0 | 28 | 2 | 3 | 4 | 2 | 0 | 1 | 10 | 2 | 1 | 3 | 3.0 |
| 3 | 0 | 51 | 1 | 4 | 3 | 5 | 1 | 3 | 8 | 10 | 8 | 8 | 5.0 |
| 1 | 0 | 57 | 7 | 7 | 3 | 3 | 5 | 1 | 13 | 11 | 4 | 3 | 6.0 |
| 10 | 1 | 20 | 1 | 4 | 4 | 0 | 0 | 2 | 1 | 8 | 0 | 0 | 2.0 |
| 9 | 0 | 74 | 6 | 10 | 14 | 9 | 5 | 2 | 8 | 10 | 8 | 2 | 5.0 |
| 8 | 1 | 42 | 1 | 18 | 11 | 0 | 0 | 2 | 1 | 9 | 0 | 0 | 1.0 |
| 7 | 0 | 79 | 10 | 11 | 9 | 7 | 5 | 11 | 11 | 10 | 5 | 0 | 7.5 |
| 6 | 1 | 2 | 2 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1.0 |
| 16 | 1 | 68 | 4 | 6 | 8 | 9 | 5 | 11 | 3 | 10 | 2 | 10 | 7.0 |
| 12 | 1 | 26 | 4 | 10 | 4 | 3 | 4 | 0 | 0 | 0 | 0 | 0 | 3.0 |
| 15 | 1 | 33 | 0 | 4 | 9 | 4 | 3 | 1 | 0 | 5 | 5 | 2 | 4.0 |
| 17 | 1 | 23 | 0 | 1 | 1 | 1 | 0 | 3 | 8 | 1 | 4 | 4 | 3.0 |
| 18 | 1 | 12 | 0 | 3 | 0 | 2 | 0 | 1 | 4 | 0 | 2 | 0 | 1.0 |

CLAIMS

1. The use of pH regulator in a method of manufacture of a medicament for the treatment of equine oral stereotypies.
2. A method of manufacture of a medicament for the treatment of equine oral stereotypies, characterised in the use of a pH regulator.
3. The use or method of either one of the preceding claims, the pH regulator being an antacid.
4. The use or method according to claim 3, the antacid comprising at least one of the group consisting sodium carbonate, sodium hydrogencarbonate, magnesium hydroxide, magnesium oxide, potassium hydroxide, calcium carbonate, calcium hydroxide, and magnesium carbonate.
5. The use or method according to either one of claims 3 or 4, the antacid being a gastric antacid.
6. The use or method according to any one of the preceding claims, the pH regulator comprising at least 50, 60, 70, 80, 90 or 95% of the therapeutically active ingredients of the medicament.
7. The use or method according to any one of claims 1-5, the pH regulator comprising at least 50, 60, 70, 80, 90 or 95% by weight of the medicament.
8. A method of treatment of an equine oral stereotypy, comprising administering to the equine a medicament according to any one of the preceding claims.



INVESTOR IN PEOPLE

Application No: GB 0000859.9
Claims searched: 1-8

Examiner: Annabel Ovens
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Patents Act 1977 Search Report under Section 17

Databases searched:

UK Patent Office collections, including GB, EP, WO & US patent specifications, in:

UK Cl (Ed.R): A5B

Int Cl (Ed.7): A61K (33/00, 33/10); A61P (25/00, 43/00)

Other: Online: PAJ, EPODOC, WPI

Documents considered to be relevant:

| Category | Identity of document and relevant passage | Relevant to claims |
|----------|---|-----------------------|
| X, E | GB 2342292 A (MARS) see page 5 lines 3-6 and page 6 line 35- page 7 line 4 and Example | 1-3 and 8 at least |
| A | WO 99/45906 A1 (TUFTS) | |
| X | US 5985891 (ROWE) see column 1 lines 12-20, column 2 lines 27-30 and column 4 line 34-column 5 line 42 | 1, 2 and 6- 8 |

X Document indicating lack of novelty or inventive step
Y Document indicating lack of inventive step if combined
with one or more other documents of same category.
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A Document indicating technological background and/or state of the art.
P Document published on or after the declared priority date but before the
filing date of this invention.
E Patent document published on or after, but with priority date earlier
than, the filing date of this application.